



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Duff, *et al.*
SERIAL NUMBER: 10/802,061 EXAMINER: Carla J. Myers
FILING DATE: March 15, 2004 ART UNIT: 1634
FOR: DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH
AN IL-1 INFLAMMATORY HAPLOTYPE

MAIL STOP AMENDMENT

Commissioner for Patents
P. O. Box 1450
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RESPONSE TO RESTRICTION REQUIREMENT

In response to the Office Action mailed June 14, 2006, Applicants elect the Group corresponding with claims 1, 3, 5 and 10-22 drawn to kits comprising a means for detecting allele 1 or allele 2 of the -511 marker of IL-1B, with traverse.

Applicants submit that, at least, the alleles of the 222/223 marker of IL-1A, the gz5/gz6 marker of IL-1A, the -889 marker of IL-1A, the +3954 marker of IL-1B, the -511 marker of IL-1B, the gaat.p33330 marker between IL-1B and IL-RN, the Y31 marker between IL-1B and IL-RN, the +2018 of IL-1RN, the +4845 of IL-1A, and the VNTR marker of IL-1RN should be examined as the same invention and not be subject to restriction. Applicants summarize the Examiner's arguments and rebut them below. Then, Applicants submit positive reasons why they above mentioned allele markers should not be restricted from each other.

The Examiner argued, on page 4 of the Office Action, that each of the above alleles is chemically, functionally and functionally distinct. The Examiner gives as an example allele 4 of the 222/223 marker of IL-1A and allele 4 of the gz5/gz6 marker of IL-1A as being distinct. Applicants respectfully disagree.

Allele 4 of the 222/223 marker of IL-1A and allele 4 of the gz5/gz6 marker of IL-1A can, and often do, describe the same gene *i.e.* IL-1A. Both of these alleles are in the same gene, and are often found together in the same haplotype: 44112332.¹

The Examiner further argued that searches for these markers would not be coextensive. Applicants submit that these searches would be coextensive. In the case of the 222/223 marker

¹ See the instant specification at page 18, lines 15-18 and the table, therein.

and gz5/gz6 alleles, one need only search the sequence of the IL-1A gene, making the searched sequence generic at the sites described above.

The Examiner also argued, on page 5 of the Office Action, that a reference that rendered allele 4 of the 222/223 marker of IL-1A anticipated or obvious would not necessarily render allele 4 of the gz5/gz6 marker of IL-1A anticipated or obvious. Applicants agree with the Examiner, but this does not render these alleles different inventions.

Applicants submit that the alleles of the 222/223 marker of IL-1A, the gz5/gz6 marker of IL-1A, the -889 marker of IL-1A, the +3954 marker of IL-1B, the -511 marker of IL-1B, the gaat.p33330 marker between IL-1B and IL-RN, the Y31 marker between IL-1B and IL-RN, the +2018 of IL-1RN, the +4845 of IL-1A, and the VNTR marker of IL-1RN should not be restricted for the following reasons. First, all of the group of allele markers described above make up a combination that, according to the MPEP, is not proper to restrict. Second, the SNP markers described above make up at most, four nucleic acid sequences. This number of nucleic acid sequences has been deemed to be proper to examine in one patent application. Third, even if the Examiner were to construe each of the above markers as a separate sequence, there are only 10 sequences. This number of nucleic acid sequences has also been deemed to be proper to examine in one patent application.

The Instant Claims are Organized into Combinations that May not be Properly Restricted.

A claim drawn to the above described allele markers, would be a combination that should not properly be restricted. The MPEP defines a combination as an organization of which a subcombination or element is a part.² A combination invention, encompassing one or more subcombinations is distinct if it can be shown that the combination as claimed (A) does not require the particulars of the subcombination as claimed for patentability (to show novelty and unobviousness), and (B) the subcombination can be shown to have utility either by itself or in another materially different combination.

As shown in claims 1,3 and 5, as pending, the combination, *i.e.* the group of allele markers described above, sets forth the details of the subcombination claims *i.e.* the allele markers separately claimed in claims 14-22. Further, the combination claims would not be patentable without specific mention of the subcombinations, *i.e.* the specific allele markers are

² MPEP § 806.05(a).

necessary to render these claims patentable. A generic reference to allele gene markers would not lead to a patentable claim. Thus, the requirements of the combination claims are necessary for the subcombination claims, meaning that these claims cannot be properly restricted, even though the subcombination elements have separate utilities.³

A combination can still be restricted by the Examiner if there is serious search burden as evidenced by separate classification, status, or field of search.⁴ The elements of the combination claims do not create a search burden by being in separate classifications, statuses, or fields of search. Further, as explained below, there is no undue burden on the Examiner to search the claims for the alleles described above.

The SNP Allelic Markers Described Encompass No More Than Four Separate Sequences and Should be Examined Together.

Nucleic acid sequences that encode different peptides have been defined as structurally distinct structural compounds. However, the markers described above are not all drawn to nucleic acid sequences that encode different peptides. Four of the markers are on the IL-1A gene, two are on the IL-1B gene, two are on the IL-1RN gene and two are between the IL-1B and IL-1RN genes. Thus, even if the Examiner were to separate the markers by what gene they were found on, each allele only changes one nucleic acid base pair out of hundreds. Thus, clearly, these molecules, when classified from genetic region in which they reside, would be considered members of the same invention.

Moreover, the Director has decided to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application.⁵ It has been determined that normally ten sequences constitute a reasonable number for examination purposes.⁶ Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction.⁷ Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together.⁸ Thus, Applicants submit, independent from the arguments above regarding the combination status of the claims, that the

³ MPEP § 806.05(c).

⁴ *Id.*

⁵ See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996).

⁶ MPEP § 803.04.

⁷ *Id.*

⁸ *Id.*

Director has created policy making it improper for the Examiner to restrict the claims to one allele. Applicants further submit that the above mentioned allele markers should all be examined in the same application.

The SNP Allelic Markers Described Could not Encompass More Than Ten Separate Sequences and Should be Examined Together.

Even if the Examiner did not deem the instant claims as combination claims, or the markers described above as encompassing only four sequences, Applicants submit that these sequences could not be construed to be more than ten nucleic acid sequences. As explained above, the Director has provided Applicants with a partial waiver to the requirements of 37 CFR 1.141 *et seq.* allowing ten sequences to be examined per application. Thus, Applicants submit that because the alleles of the 222/223 marker of IL-1A, the gz5/gz6 marker of IL-1A, the -889 marker of IL-1A, the +3954 marker of IL-1B, the -511 marker of IL-1B, the gaat.p33330 marker between IL-1B and IL-RN, the Y31 marker between IL-1B and IL-RN, the +2018 of IL-1RN, the +4845 of IL-1A, and the VNTR marker of IL-1RN encompass only ten sequences for Restriction purposes, these allele markers should be examined as the same invention and not be subject to restriction.